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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/911,050	07/23/2001	James L. Bullington	ORT-1477	3229

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EXAMINER
ROBINSON, BINTA M

ART UNIT	PAPER NUMBER
1625	

DATE MAILED: 08/19/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/911,050	Applicant(s) BULLINGTON ET AL.	
	Examiner Binta M. Robinson	Art Unit 1625	

-- Th MAILING DATE of this communication appears on th cover sheet with th correspond nc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *54 and 57* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *54, 57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Detailed Action

The 101 double patenting rejection of claims 1-51, 53, 55, 56, 57, and 58, the 112 first paragraph rejection and 112, second paragraph rejection of claims 55-56 are withdrawn in light of applicant's amendment at paper no. 6/a.

(old rejection)

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 54 and 57 are rejected under 35 U.S.C. 112, first paragraph, because the specification, does not reasonably provide enablement for the method of treating all diseases in claims 56 and 58, many of which are unrelated. The diseases claimed cover such a broad spectrum of diseases that are so unrelated. One drug can not treat various diseases with different mechanisms. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The claims as recited are broader than the scope of enablement.

The applicant is referred to ***In re Wands***, 858 f.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) which includes the incorporation of the 8 factors recited in ***Ex parte*** Foreman 230 USPQ 546 (Bd. Of App. And Inter 1986).

There are many factors to be considered when determining whether there

is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include 1)the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art 6) the amount of direction provided by the inventor 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In re Wands, 858 F. 2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

In terms of the breadth of the claims, R6 of formula I can equal aryl, 3-piperidyl, N-substituted 3-piperidyl, N-substituted 2-pyrrolidinyl methylene, as well as the nonheterocyclic rings claimed, R' and R" of both formulas I and II can come together to form the heterocyclic rings claimed as well as the non-heterocyclic rings claimed, R1 and R2 of formulas I and II can come together to form oxadiazole, R7 of formulas I and II can be 2-thieno and 3-thieno as well as the non-heterocyclic moieties claimed, R9 of formula II can be cyclic carbonate as well as lactone, and RI and RII can be heterocyclyl optionally substituted with the moieties claimed.

In terms of the nature of the invention, these compounds are useful as calcium channel antagonists with cardiovascular, antiasthmatic and antibronchoconstriction activity.

In terms of the fifth Wands factor, the level of predictability in the art was low since there is large variation in Nitrendipine Binding activity with small changes in structure. For example, compound 3 of formula I in Table 1, differs from compound 6

at the R1 and R5 moieties. In compound 3, R1 is CL and R5 is F. In compound 6, R1 is H, R5 is Cl. For compound 1, Nitrendipine Binding is 160 nM, and for compound 6, Nitrendipine binding is 0.045 nM. Additionally, compounds 2 and 3 appear to have the same structure, however, Nitrendipine binding for compound 2 is 0.043 nM and for compound 3 is 160 nM. The compound have also not been tested for their effects on the specific diseases claimed. In terms of the sixth Wands factor, the amount of direction provided by the inventor is poor, because the applicant does not conduct tests for compounds of formulas I and II where R1 and R2 come together to form oxadiazole, where R7 is 2-thieno or 3-thieno or formula II where the substituents on R9 are other optionally substituted heterocyclic rings other than lactone, cyclic carbonate, piperidine, or pyridyl.

The applicant does not test a representative breadth of compounds encompassing the moieties that these particular radicals can be. In terms of the 8th Wands factors, undue experimentation would be required to make or use the invention based on the content of the disclosure due to the breadth of the claims, the level of predictability in the art of the invention, and the poor amount of direction provided by the inventor. Taking the above factors into consideration, it is not seen where the instant claim is enabled by the instant application.

(new rejection)

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is

most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 54 and 57 are rejected under 35 U.S.C. 112, first paragraph, because the specification, does not reasonably provide enablement for R' and R" of formula I coming together to form all of the heterocyclic rings claimed, R1 and R2 of formulas I and II coming together to form an oxadiazole, RI and RII substituents on R9 of the compounds of formula II coming together to form heterocyclyl, heterocyclyl being optionally substituted with halogen, cyano, NO2, or lactone. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The claims as recited are broader than the scope of enablement.

The applicant is referred to ***In re Wands***, 858 f.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) which includes the incorporation of the 8 factors recited in ***Ex parte*** Foreman 230 USPQ 546 (Bd. Of App. And Inter 1986).

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include 1)the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art 6) the amount of direction provided by the inventor 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In re Wands, 858 F. 2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

In terms of the breadth of the claims, R6 of formula I can equal aryl, 3-piperidyl, N-substituted 3-piperidyl, N-substituted 2-pyrrolidinyl methylene, as well as the nonheterocyclic rings claimed, R' and R" of both formulas I and II can come together to form the heterocyclic rings claimed as well as the non-heterocyclic rings claimed, R1 and R2 of formulas I and II can come together to form oxadiazole, R7 of formulas I and II can be 2-thieno and 3-thieno as well as the non-heterocyclic moieties claimed, R9 of formula II can be cyclic carbonate as well as lactone, and RI and RII can be heterocyclyl optionally substituted with the moieties claimed.

In terms of the nature of the invention, these compounds are useful as calcium channel antagonists with cardiovascular, antiasthmatic and antibronchoconstriction activity.

In terms of the fifth Wands factor, the level of predictability in the art was low since there is large variation in Nitrendipine Binding activity with small changes in structure. For example, compound 3 of formula I in Table 1, differs from compound 6 at the R1 and R5 moieties. In compound 3, R1 is CL and R5 is F. In compound 6, R1 is H, R5 is Cl. For compound 1, Nitrendipine Binding is 160 nM, and for compound 6, Nitrendipine binding is 0.045 nM. Additionally, compounds 2 and 3 appear to have the same structure, however, Nitrendipine binding for compound 2 is 0.043 nM and for compound 3 is 160 nM. In terms of the sixth Wands factor, the amount of direction provided by the inventor is poor, because the applicant does not conduct tests for compounds of formulas I and II where R1 and R2 come together to form oxadiazole, where R7 is 2-thieno or 3-thieno or formula II where the substituents on R9 are other

optionally substituted heterocyclic rings other than lactone, cyclic carbonate, piperidine, or pyridyl.

The applicant does not test a representative breadth of compounds encompassing the moieties that these particular radicals can be. In terms of the 8th Wands factors, undue experimentation would be required to make or use the invention based on the content of the disclosure due to the breadth of the claims, the level of predictability in the art of the invention, and the poor amount of direction provided by the inventor. Taking the above factors into consideration, it is not seen where the instant claim is enabled by the instant application.

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 54 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claim 54 recites the limitation "R^{I} and R^{III}" in line 5, page 5 of the amendment 6/A. There is insufficient antecedent basis for this limitation in the claim.

B. In claim 54, line 18, page 3 of the amendment 6/A, the phrase "as applicable" is indefinite. What does the applicant mean by this phrase?

Response to Applicant's Remarks – 112, first paragraph rejection

The applicants allege that the disclosure fully enables the claimed methods of treating the diseases claimed asserting that the use of calcium channel blockers in treating disorders such as hypersensitivity, allergy, asthma and bronchospasm is well

known in the art and that these compound exert their effects locally. However, hypersensitivity, allergy, asthma, and bronchospasm require different mechanisms, and antagonists. The specification does not disclose the effects of these compounds on each of these diseases. There is no reasonable assurance that such a diverse genus of compounds would possess the diverse properties claimed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

3. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Binta M. Robinson whose telephone number is (703) 306-5437. The examiner can normally be reached on M-F (9:30-6:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Alan Rotman can be reached on (703)308-4698. The fax phone numbers

for the organization where this application or proceeding is assigned are (703)308-7922 for regular communications and (703)308-7922 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703)308-0193.

Binta Robinson

August 15, 2002

Alan L. Rotman

ALAN L. ROTMAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600